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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/594,101	05/22/2007	Didier Cataldo	22394	7348

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HOFFMANN-LA ROCHE INC.
PATENT LAW DEPARTMENT
340 KINGSLAND STREET
NUTLEY, NJ 07110

EXAMINER	
SZNAIDMAN, MARCOS L	
ART UNIT	PAPER NUMBER
1611	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/594,101	CATALDO ET AL.	
	Examiner	Art Unit	
	MARCOS SZNAIDMAN	1611	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 May 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5 pages / 02/07/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This office action is in response to applicant's reply filed on May 28, 2008.

Election/Restrictions

Applicant's election without traverse of the species: 5-biphenyl-4-yl-5-[4-(4-nitro-phenyl)-piperazin-1-yl]pyrimidine-2,4,6-trione (Ro 28-2653) in the reply filed on May 28, 2008 is acknowledged.

Status of Claims

Claims 1-3 are currently pending and are the subject of this office action.

Claims 1-3 are presently under examination.

Priority

The present application is a 371 of PCT/EP05/03345 filed on 003/31/2005, and claims priority to foreign application: EPO 04007920.4 filed on 04/01/2004.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1 and 3 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter

which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

Claims 1 and 3 recite a method for treating bronchial inflammatory diseases comprising administering to a patient a pharmacologically effective amount of a trioxopyrimidine having an inhibitory activity against MMP-1 (matrix metalloprotease-1), MMP-2, MMP-3, MMP-9 and MMP-14 defined as:

1- an IC50 value of less than 5 micromolar for MMP-2, MMP-9 and MMP-14,

2- a ratio of more than 100 for the IC50 values of MMP-1/MMP-2, MMP-1/MMP-9, and MMP-1/MMP-14; and

3- a ratio of more than 10 for the IC50 values of MMP-3/MMP-2, MMP-3/MMP-9, and MMP-3/MMP-14.

M.P.E.P. #2163 states: "An applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention....one must define a compound by 'whatever characteristics sufficiently distinguish it'. A lack of adequate written description issue also arises if the knowledge and level of skill in the art would not permit one skilled in the art to immediately envisage the product claimed from the disclosed process".

M.P.E.P. 2163 II-A-3-a ii) states: "The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus (see i) (C), above). See Eli Lilly, 119 F.3d at 1568, 43 USPQ2d at 1406.

A "representative number of species" means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. The disclosure of only one species encompassed within a genus adequately describes a claim directed to that genus only if the disclosure "indicates that the patentee has invented species sufficient to constitute the gen[us]." See Enzo Biochem, 323 F.3d at 966, 63 USPQ2d at 1615; Noelle v. Lederman, 355 F.3d 1343, 1350, 69 USPQ2d 1508, 1514 (Fed. Cir. 2004) (Fed. Cir. 2004)("[A] patentee of a biotechnological invention cannot necessarily claim a genus after only describing a limited number of species because there may be unpredictability in the results obtained from species other than those specifically enumerated."). "A patentee will not be deemed to have invented species sufficient to constitute the genus by virtue of having disclosed a single species when ... the evidence indicates ordinary artisans could not predict the operability in the invention of any species other than the

one disclosed." In re Curtis, 354 F.3d 1347, 1358, 69 USPQ2d 1274, 1282 (Fed. Cir. 2004).

The specification (see page 4) and claim 2, recite only five compounds with the limitations of claim 1. There are an enormous amount of compounds (some known, some still unknown) that could potentially be encompassed by the limitations of claim 1.

Given the broad scope of the claimed subject matter, applicant has not provided sufficient written description that would allow the skilled artisan to recognize that applicant was in possession of the claimed structures encompassed by the limitations of claim 1, except for the five compounds recited in claim 2 or page 4 of the specification.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.

4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1 and 2 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kumagai et. al. (The Journal of Immunology (1999) 162:4212-4219), in view of Lein et. al. (Oncogene (2002) 21:2089-2096).

Claims 1 and 2 recite a method for treating bronchial inflammatory diseases comprising administering to a patient a pharmacologically effective amount of 5-biphenyl-4-yl-5-[4-(4-nitro-phenyl)-piperazin-1-yl]pyrimidine-2,4,6-trione (Ro 28-2653) (species elected).

For claims 1 and 2, Kumagai teaches that inhibition of MMPs, and in particular MMP-2 and MMP-9, are crucial for the treatment of bronchial asthma (a bronchial

inflammatory disease) (see abstract, last four lines and page 4218, left column, last paragraph).

Kumagai et. al do not teach the treatment of a bronchial inflammatory disease with Ro 28-2653. However, Lein et. al. teach that Ro 28-2653 is a MMP inhibitor with high selectivity for MMP-2 and MMP-9 (see abstract, lines 3 through 6).

Since Kumagai et. al. teach that bronchial asthma (a bronchial inflammatory disease) can be treated by inhibiting MMP-2 and MMP-9, and since Lein et. al. teach that Ro 28-2653 inhibits MMP-2 and MMP-9, at the time of the invention it would have been prima facie obvious for a person of ordinary skill in the art to treat any bronchial inflammatory disease with Ro 28-2653, with the motivation of better treating bronchial inflammatory diseases, thus resulting in the practice of claims 1-2 with a reasonable expectation of success.

Claim 3 is rejected under 35 U.S.C. 103(a) as being unpatentable over Kumagai et. al. (The Journal of Immunology (1999) 162:4212-4219), in view of Lein et. al. (Oncogene (2002) 21:2089-2096) as applied to claims 1-2 above, and further in view of Aki et. al. (Journal of Pharmaceutical Sciences (2001) 90: 1186-1197).

Claim 3, further limits claim 1, wherein Ro 28-2653 (species elected) is complexed with water soluble cyclodextrin.

Kumagai et. al. and Lein et. al. teach all the limitations of claim 3, except for the complexation of Ro 28-2653 (a trioxopyrimidine) with a water-soluble cyclodextrin.

However, Aki et. al. teach the formation of complexes between barbiturates (trioxopyrimidines) and 2-hydroxypropyl-beta-cyclodextrin (a water-soluble cyclodextrin).

Since Aki et al. further teach that trioxopyrimidines can be complexed with water-soluble cyclodextrins, at the time of the invention it would have been *prima facie* obvious for a person of ordinary skill in the art to further complex Ro 28-2653 (a trioxopyrimidine), with the motivation of giving this compound a better water solubility, thus resulting in the practice of claim 3 with a reasonable expectation of success.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MARCOS SZNAIDMAN whose telephone number is (571)270-3498. The examiner can normally be reached on Monday through Thursday 8 AM to 6 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sharmila G. Landau can be reached on 571 272-0614. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/MARCOS SZNAIDMAN/
Examiner, Art Unit 1611
August 5, 2008

/Sharmila Gollamudi Landau/

Supervisory Patent Examiner, Art Unit 1611